

Claims

- Sub A1 7
1. A method for treating myocardial infarction comprising:
administering to a subject in need of such treatment an Akt molecule in an amount effective to inhibit cardiac tissue necrosis in the subject.
 - 5 2. The method of claim 1, wherein the cardiac tissue necrosis is mediated by increased apoptotic cell-death of a cardiomyocyte.
 3. The method of claim 1, wherein the cardiac tissue necrosis is mediated by increased apoptotic cell-death of a cardiac tissue endothelial cell.
 4. The method of claim 1, wherein the Akt molecule is administered acutely.
 - 10 5. The method of claim 4, wherein the Akt molecule is administered acutely into the apical and anterolateral free wall of the heart.
 6. The method of claims 1-5, further comprising co-administering an anti-atherosclerotic agent used in the treatment of an atherosclerotic condition.
 7. The method of claim 6, wherein the anti-atherosclerotic agent is selected from the group
15 consisting of a HMG-CoA reductase inhibitor, a diuretic, an antiadrenergic agent, a vasodilator, a calcium channel antagonist, an angiotensin-converting enzyme inhibitor, an angiotensin II antagonist, and a clot dissolver.
 - Sub A2 7 8. The method of claims 1-5, further comprising co-administering a growth factor.
 9. The method of claim 8, wherein the growth factor is IGF-1.
 - 20 10. A method for inhibiting apoptotic cell-death of cardiomyocytes, comprising:
contacting an Akt molecule with a cardiomyocyte under conditions to permit entry of the Akt molecule into the cardiomyocyte,
wherein the Akt molecule is present in an amount effective to inhibit apoptotic cell-death of the cardiomyocyte.
 - 25 11. The method of claim 10, wherein the contacting of an Akt molecule with a cardiomyocyte comprises acute administration of the Akt molecule.
 12. The method of claim 10, wherein the contacting of an Akt molecule with a cardiomyocyte comprises prophylactic administration of the Akt molecule.
 13. The method of claim 10, wherein the cardiomyocyte is part of a tissue or an organ to be
30 transplanted.
 14. The method of claim 13, wherein the contacting of an Akt molecule with a cardiomyocyte comprises acute administration of the Akt molecule.

15. The method of claim 14, wherein the contacting of an Akt molecule with a cardiomyocyte comprises prophylactic administration of the Akt molecule.

16. A method for inhibiting apoptotic cell-death of vascular endothelial cells, comprising:

contacting an Akt molecule with a vascular endothelial cell under conditions to permit entry of the Akt molecule into the vascular endothelial cell,

wherein the Akt molecule is present in an amount effective to inhibit apoptotic cell-death of the vascular endothelial cell.

17. The method of claim 16, wherein the vascular endothelial cell is part of a tissue or an organ to be transplanted.

18. The method of claim 17, wherein the contacting of an Akt molecule with a cardiomyocyte comprises acute administration of the Akt molecule.

19. The method of claim 17, wherein the contacting of an Akt molecule with a cardiomyocyte comprises prophylactic administration of the Akt molecule.

20. The method of claims 16-19, further comprising co-administering a growth factor.

21. The method of claim 20, wherein the growth factor is VEGF.

22. A method for treating a condition associated with increased apoptotic cell-death of vascular endothelial cells, comprising:

administering to a subject in need of such treatment an Akt molecule in an amount effective to inhibit increased apoptotic cell-death of vascular endothelial cells.

23. The method of claim 22, wherein the condition is characterized by lesions of a blood vessel wall.

24. A method for inhibiting apoptotic cell-death of a skeletal myocyte, comprising:

contacting an Akt molecule with a skeletal myocyte under conditions to permit entry of the Akt molecule into the skeletal myocyte,

wherein the Akt molecule is present in an amount effective to inhibit apoptotic cell-death of the skeletal myocyte.

25. The method of claim 24, wherein the skeletal myocyte is part of a tissue or an organ to be transplanted.

26. A method for treating a condition associated with increased apoptotic cell-death of a skeletal myocyte, comprising:

administering to a subject in need of such treatment an Akt molecule in an amount effective to inhibit increased apoptotic cell-death of a skeletal myocyte.

27. The method of claim 26, wherein the condition is selected from the group consisting of muscular dystrophy, spinal muscular atrophy, anabolic steroid-induced muscle injury, skeletal muscle oxidative stress, physical exercise, and unloading-induced skeletal muscle atrophy.

28. A composition comprising:

5 an isolated human Akt nucleic acid operably linked to a gene expression sequence, wherein the gene expression sequence permits expression of the Akt nucleic acid in a eukaryotic cell selected from the group consisting of a cardiomyocyte, a skeletal muscle cell and a vascular endothelial cell, and
a vector associated with the Akt nucleic acid.

10 29. The composition of claim 28, wherein the eukaryotic cell is a cardiomyocyte.

30. The composition of claim 28, wherein the eukaryotic cell is a vascular endothelial cell.

31. The composition of claim 28, wherein the eukaryotic cell is a skeletal myocyte.

32. The composition of claim 28, wherein the vector is an adenoviral vector.

33. The composition of claim 28, further comprising an anti-atherosclerotic agent selected
15 from the group consisting of a HMG-CoA reductase inhibitor, a diuretic, an antiadrenergic agent, a vasodilator, a calcium channel antagonist, an angiotensin-converting enzyme (ACE) inhibitor, an angiotensin II antagonist, and a clot dissolver.

34. A method of screening for an inhibitory agent that inhibits apoptotic cell-death of cells, comprising the steps of:

20 (a) inducing apoptotic cell-death in a test sample containing one or more types of cells;

(b) contacting a putative inhibitory agent with the cells of the test sample under conditions to permit entry of the agent into the cell;

(c) determining a test sample index cell number; and

(d) comparing the test sample index cell number with a control index cell number of a
25 control sample, wherein the control sample has been contacted with an Akt molecule under conditions to permit entry of the Akt molecule into the cell, and

wherein the index cell number of the test sample as compared with the equivalent index cell number of the control sample is indicative of the inhibitory activity of the test agent in inhibiting death of the cells.

30 35. The method of claim 34, wherein the screening is performed *in vitro*.

36. The method of claim 35, wherein the cells are selected from the group consisting of cardiomyocytes, skeletal muscle cells and vascular endothelial cells.

37. The method of claim 34, wherein the screening is performed *in vivo*.
38. The method of claim 37, wherein the cells are from a subject tissue selected from the group consisting of myocardium, skeletal musculature and vascular endothelium.

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